

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Whitman *et al.*

Serial No.:

Filed: 01/11/02

Entitled: **METHODS AND COMPOSITIONS FOR MODULATING TGF-BETA SUPERFAMILIY SIGNALLING**

Group No.:

Examiner:

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents

Washington, D.C. 20231

CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this document and any documents referred to as enclosed therein are being deposited with the U.S. Postal Service on this date **January 11, 2002** in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number **EL 837 033 644 US** addressed to: **Box Patent Application, Assistant Commissioner For Patents, Washington, D.C. 20231.**

Dated: 1-11-02

By: Susan M. McClintock
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Sir or Madam:

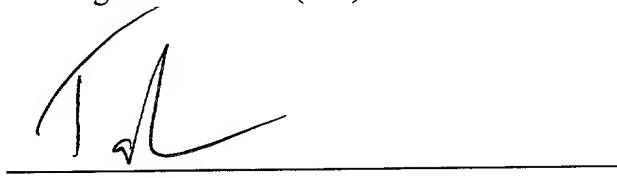
Prior to the examination of this Application, Applicants respectfully request that the following amendments be entered.

IN THE CLAIMS:

Please cancel Claims 17-29.

REMARKS

Claims 1-29 are filed in the accompanying Divisional Application. The above amendment cancels Claims 17-29. Claims 17-29 have not been cancelled for reasons related to patentability. The claims have been cancelled solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),¹ and without waiving the right to prosecute the cancelled claims (or similar claims) in the future. As such, Claims 1-16 are currently pending in this Application. a copy of the pending claims is attached to this communication for the Examiner's convenience. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.



Dated: January 11, 2002

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¹ 65 Fed. Reg. 54603 (Sept., 8, 2000).

PENDING CLAIMS

1. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

(a) providing a cell having:

(i) a reporter gene operably linked to a DNA-binding-protein recognition site;

(ii) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of Smad2 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and

(iii) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a gene activating moiety;

(b) exposing said cell to said compound; and

(c) measuring reporter gene expression in said cell, a change in said reporter gene expression indicating said compound is capable of modulating TGF- β superfamily signalling.

2. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

(a) providing a cell having:

(i) a reporter gene operably linked to a DNA-binding-protein recognition site;

(ii) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and

(iii) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of Smad2 covalently bonded to a gene activating moiety;

(b) exposing said cell to said compound; and

(c) measuring reporter gene expression in said cell, a change in said reporter gene expression indicating said compound is capable of modulating TGF- β superfamily signalling.

3. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

(a) providing a cell having:

(i) a reporter gene operably linked to a DNA-binding-protein recognition site;

(ii) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of Smad3 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and

(iii) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a gene activating moiety;

(b) exposing said cell to said compound; and

(c) measuring reporter gene expression in said cell, a change in said reporter gene expression indicating said compound is capable of modulating TGF- β superfamily signalling.

4. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

(a) providing a cell having:

(i) a reporter gene operably linked to a DNA-binding-protein recognition site;

(ii) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and

(iii) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of Smad3 covalently bonded to a gene activating moiety;

- (b) exposing said cell to said compound; and
- (c) measuring reporter gene expression in said cell, a change in said reporter gene expression indicating said compound is capable of modulating TGF- β superfamily signalling.

5. A cell for detecting a compound capable of modulating TGF- β superfamily signalling, said cell having:

- (a) a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of Smad2 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and
- (c) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a gene activating moiety.

6. A cell for detecting a compound capable of modulating TGF- β superfamily signalling, said cell having:

- (a) a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and
- (c) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of Smad2 covalently bonded to a gene activating moiety.

7. A cell for detecting a compound capable of modulating TGF- β superfamily signalling, said cell having:

- (a) a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of Smad3 covalently bonded to a binding moiety,

said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and

(c) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a gene activating moiety.

8. A cell for detecting a compound capable of modulating TGF- β superfamily signalling, said cell having:

(a) a reporter gene operably linked to a DNA-binding-protein recognition site;

(b) a first fusion gene capable of expressing a first fusion protein, said first fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site; and

(c) a second fusion gene capable of expressing a second fusion protein, said second fusion protein comprising a polypeptide fragment of Smad3 covalently bonded to a gene activating moiety.

9. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

(a) providing a first polypeptide, said first polypeptide comprising a polypeptide fragment of FAST-1;

(b) providing a second polypeptide, said second polypeptide comprising a polypeptide fragment of Smad2;

(c) exposing said first polypeptide to said second polypeptide and to said compound; and

(d) measuring the level of interaction between said first polypeptide and said second polypeptide, an alteration in said level of interaction indicating said compound is capable of modulating TGF- β superfamily signalling.

10. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a first polypeptide, said first polypeptide comprising a polypeptide fragment of Smad2;
- (b) providing a second polypeptide, said second polypeptide comprising a polypeptide fragment of FAST-1;
- (c) exposing said first polypeptide to said second polypeptide and to said compound; and
- (d) measuring the level of interaction between said first polypeptide and said second polypeptide, an alteration in said level of interaction indicating said compound is capable of modulating TGF- β superfamily signalling.

11. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a first polypeptide, said first polypeptide comprising a polypeptide fragment of FAST-1;
- (b) providing a second polypeptide, said second polypeptide comprising a polypeptide fragment of Smad3;
- (c) exposing said first polypeptide to said second polypeptide and to said compound; and
- (d) measuring the level of interaction between said first polypeptide and said second polypeptide, an alteration in said level of interaction indicating said compound is capable of modulating TGF- β superfamily signalling.

12. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a first polypeptide, said first polypeptide comprising a polypeptide fragment of Smad3;
- (b) providing a second polypeptide, said second polypeptide comprising a polypeptide fragment of FAST-1;
- (c) exposing said first polypeptide to said second polypeptide and to said compound; and

(d) measuring the level of interaction between said first polypeptide and said second polypeptide, an alteration in said level of interaction indicating said compound is capable of modulating TGF- β superfamily signalling.

13. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) providing a first fusion protein, said first fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site;
- (c) providing a second fusion protein, said second fusion protein comprising a polypeptide fragment of Smad2 covalently bonded to a gene activating moiety;
- (d) exposing said first fusion protein to said second fusion protein, to said reporter gene, and to said compound; and
- (e) measuring the reporter gene expression, a change in said reporter gene expression indicating a compound capable of modulating TGF- β superfamily signalling.

14. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) providing a first fusion protein, said first fusion protein comprising a polypeptide fragment of Smad2 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site;
- (c) providing a second fusion protein, said second fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a gene activating moiety;
- (d) exposing said first fusion protein to said second fusion protein, to said reporter gene, and to said compound; and

(e) measuring the reporter gene expression, a change in said reporter gene expression indicating a compound capable of modulating TGF- β superfamily signalling.

15. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) providing a first fusion protein, said first fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site;
- (c) providing a second fusion protein, said second fusion protein comprising a polypeptide fragment of Smad3 covalently bonded to a gene activating moiety;
- (d) exposing said first fusion protein to said second fusion protein, to said reporter gene, and to said compound; and
- (e) measuring the reporter gene expression, a change in said reporter gene expression indicating a compound capable of modulating TGF- β superfamily signalling.

16. A method for detecting a compound capable of modulating TGF- β superfamily signalling, said method comprising the steps of:

- (a) providing a reporter gene operably linked to a DNA-binding-protein recognition site;
- (b) providing a first fusion protein, said first fusion protein comprising a polypeptide fragment of Smad3 covalently bonded to a binding moiety, said binding moiety capable of specifically binding to said DNA-binding-protein recognition site;
- (c) providing a second fusion protein, said second fusion protein comprising a polypeptide fragment of FAST-1 covalently bonded to a gene activating moiety;
- (d) exposing said first fusion protein to said second fusion protein, to said reporter gene, and to said compound; and

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- (e) measuring the reporter gene expression, a change in said reporter gene expression indicating a compound capable of modulating TGF- β superfamily signalling.

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